Congenital Disorders of Glycosylation (CDG)

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2025 Second Round Interim Report

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Please Note:

- This interim report is intended for participants of the ERNDIM CDG scheme. The contents should not be used for any publication without permission of the Scientific Advisor.
- This is an interim report, and it includes provisional scores only. All scores are subject to change following moderation at the Scientific Advisory Board meeting in autumn of this year. For final scores and performance data the ERNDIM CDG Annual Report should be referred to.
- The fact that your laboratory participates in this scheme is not confidential, however, the raw data and performance scores are confidential and will only be shared within ERNDIM for the purpose of evaluating your laboratories performance, unless ERNDIM is required to disclose performance data by a relevant government agency. For details, please see the ERNDIM Privacy Policy on www.erndim.org.

1. Results Submission

Results were submitted to the online results website (cscq.hcuge.ch/cscq/ERNDIM/) which is hosted and maintained by CSCQ. The submission deadline for the second round (samples CDG-PP-2025-D, -E and -F) was 8th Sep 2025.

From the 57 laboratories registered for the 2025 CDG scheme 51 labs (89%) submitted results for the second round.

2. Scoring scheme

In agreement with ERNDIM rules, we applied a scoring system of 2+2:

Technical aspects: 1 point for identification of an abnormal profile and 1 point for correct identification of the profile as type I or II.

Diagnostic suggestions: This section should be filled for scoring. Just referring to a specialised lab is insufficient. If required, advice can be obtained from a reference laboratory or in collaboration with a clinical colleague. For normal profiles 2 points are scored. For abnormal profiles, comments should be made on the possibility of the presence of a secondary cause in light of the clinical indication. In addition, the right suggestions should be made for the next step in the diagnostic process that eventually will lead to the genetic defect. Scoring for this part is not so straightforward, but we tried to keep it as consistent as possible. The maximum score achievable with full submission for all samples is 24, while a maximum of 12 points are available for labs that only submitted results for the first or second round. The level for satisfactory performance is 17 points.

[1] **If this Interim Report is not Version 1 for this scheme year, go to APPENDIX 2 (page 5) for details of the changes made since the last version of this document.**

For the 2022 scheme onwards labs that only submit results for 3 or fewer samples in a scheme year will be classed as partial submitters and their performance will not be evaluated. This information is included in the CDG scheme instructions for 2022 onwards. Partial submitters receive a formal Non-submitter letter notifying them of this status and their certificate of participation shows them as not submitting results for the relevant scheme. As the number of participants in the CDG scheme are limited due to the nature of the EQA samples, ERNDIM reserves the right to exclude participants that are classed as partial/non-submitters for 2 out of 3 registered years (i.e., persistent partial and non-submitters) from the scheme.

Satisfactory performance requires the absence of any "critical error", which is defined as an error resulting from seriously misleading analytical findings and/or interpretations with serious clinical consequences for the patient. For the 2025 CDG scheme, any critical errors will be agreed at the meeting of the Scientific Advisory Board on 27th and 28th November 2025, and details of these will be included in the 2025 CDG Annual Report.

a. Appeals

If your laboratory is classed as having poor performance at the end of the 2025 scheme and you wish to appeal against this classification, please use the link given in the Performance Support letter you will be sent, to submit your appeal request. The online form should be completed with full details of the reason for your appeal and submitted within one month of receiving your Performance Support Letter. Please note that only appeals submitted using the online response form will be considered.

3. Results of samples and evaluation of reporting

The shipped samples were from (CDG) patients and from controls. The final results of the three second-round samples with respect to CDG are summarised in Table 1 below.

Table 1: Samples in the second round of the 2025 scheme

Sample	Clinical Information	Sex	Age	Diagnosis
CDG-PP-2025-D	Cerebellar hypoplasia, dysmorphic features, nystagmus.	F	4 years	PMM2-CDG
CDG-PP-2025-E	Autistic behaviour spectrum.	M	7 years	Transferrin variant
CDG-PP-2025-F	Muscular hypotonia, intellectual disability, scoliosis.	F	11 years	PMM2-CDG

All submitted results are treated as confidential information and are only shared with ERNDIM approved persons for evaluation and reporting purposes.

For the laboratories that reported their method (52/57), isoelectric focusing was still the most frequently employed technique (15/52), just closely followed by HPLC (14/52) and CE (11/52), then mass spectrometry (10/52), and other methods (1/52).

Table 2: Scoring of the second-round samples in the 2025 scheme

Sample	No of returns	Technical Aspects (%)	Diagnostic Suggestions (%)	Total (%)
CDG-PP-2025-D	51	98.0	90.2	94.1
CDG-PP-2025-E	51	91.2	88.2	89.7
CDG-PP-2025-F	51	97.1	85.3	91.2

The full anonymised results for all labs that submitted results are given in APPENDIX 1 on page 4 of this report.

3.1. CDG-PP-2025-D: Type 1 – PMM2-CDG

A type I transferrin glycoform profile was identified and interpreted as abnormal by most laboratories, resulting in a total proficiency score of 94.1%. The pattern corresponded to a classical type I profile, without major differences between the analytical methods used.

The clinical information provided is compatible with PMM2-CDG, the most frequent CDG-I subtype. Therefore, when a type I profile is observed in this context, PMM2-CDG should be considered as the most likely diagnosis. The high total score reflects not only the correct identification of the abnormal type I profile but also the provision of appropriate diagnostic recommendations, which were mainly focused on genetic studies and enzymatic analysis of phosphomannomutase activity in leukocytes. Correct identification of the type I abnormal profile, together with the suggestion of PMM2-CDG as a possible diagnosis and the recommendation of appropriate genetic studies, was required for full scoring.

3.2. CDG-PP-2025-F: Transferrin variant

Most laboratories using IEF or CE reported an abnormal transferrin glycoform profile, either directly suggesting a protein polymorphism or describing it as an abnormal type II pattern, resulting in a total proficiency score of

89.7%. The polymorphism was detectable only by IEF or CE, but not by HPLC, Western blot, or mass spectrometry.

For laboratories reporting an abnormal profile, recommending neuraminidase treatment as a confirmatory step was required for full scoring. Two laboratories using CE and one participant using IEF reported a normal profile, misinterpreting the transferrin glycoform pattern, while one participant incorrectly assigned the sample as type I CDG.
Although the presence of a transferrin polymorphism is clinically benign, it can complicate the interpretation of the glycoform profile and should always be ruled out before considering a pathological cause.

3.3. CDG-PP-2025-F: Type 1 – PMM2-CDG

A type I transferrin glycoform profile was detected and classified as abnormal by almost all laboratories, resulting in a total proficiency score of 91.2%. The profile exhibited the typical characteristics of a classical type I pattern, and comparable results were obtained across the different analytical methods employed.

The clinical presentation was compatible with PMM2-CDG, the most common subtype of CDG-I. In such cases, the observation of a type I profile should prompt consideration of PMM2-CDG as a primary diagnostic possibility. The high total score indicates that most laboratories not only recognised the abnormal pattern but also provided suitable diagnostic recommendations, primarily focused on genetic testing and assessment of phosphomannomutase activity in leukocytes. Accurate interpretation of the abnormal profile, together with the suggestion of PMM2-CDG as a possible diagnosis and the inclusion of appropriate diagnostic guidance, was required for full scoring.

4. Questions, Comments and Suggestions

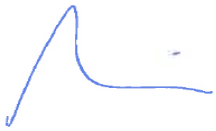
If you have any questions, comments or suggestions in addition to specific user comments please contact the ERNDIM Administration Office (admin@erndim.org).

5. Confidentiality Statement

This interim report is intended for participants of the ERNDIM Congenital Disorders of Glycosylation scheme. The contents of this report or data derived from the use or analysis of ERNDIM EQA materials must not be used in written publications or oral presentations unless the explicit prior consent of ERNDIM has been granted.

Dr Dulce Quelhas

Scientific Advisor



Dr Blai Morales

Deputy Scientific Advisor

APPENDIX 1. **Detailed scores for submitting laboratories**

Sample ID	Technical				Advice				Total score (Max 12)
	D	E	F	Total	D	E	F	Total	
Average score / Lab ID	1.96	1.82	1.94		1.80	1.76	1.71		
1	2	2	2	**6**	2	2	2	**6**	**12**
2	2	2	2	**6**	2	2	2	**6**	**12**
3	2	2	2	**6**	2	2	2	**6**	**12**
4	2	2	2	**6**	2	1	2	**5**	**11**
5									**No results submitted**
6	2	2	2	**6**	2	2	2	**6**	**12**
7	2	2	2	**6**	2	2	2	**6**	**12**
8	2	2	2	**6**	2	2	1	**5**	**11**
9	2	2	2	**6**	1	2	1	**4**	**10**
10	2	1	2	**5**	1	2	1	**4**	**9**
11	2	2	2	**6**	2	2	2	**6**	**12**
12	2	2	2	**6**	1	1	1	**3**	**9**
13	2	2	2	**6**	2	2	2	**6**	**12**
14	2	0	2	**4**	2	0	2	**4**	**8**
15									**No results submitted**
16	2	2	2	**6**	2	2	2	**6**	**12**
17	2	2	2	**6**	2	2	2	**6**	**12**
18	2	2	2	**6**	2	2	2	**6**	**12**
19	2	2	2	**6**	2	2	2	**6**	**12**
20	2	2	2	**6**	2	2	2	**6**	**12**
21	2	2	2	**6**	2	2	2	**6**	**12**
22	2	2	2	**6**	2	2	2	**6**	**12**
23	2	2	2	**6**	1	2	1	**4**	**10**
24	2	2	2	**6**	1	2	1	**4**	**10**
25	2	2	2	**6**	1	2	2	**5**	**11**
26	2	2	2	**6**	1	2	1	**4**	**10**
27	2	2	2	**6**	2	2	1	**5**	**11**
28	2	2	2	**6**	2	2	2	**6**	**12**
29	2	2	2	**6**	2	2	2	**6**	**12**
30	2	2	2	**6**	2	1	2	**5**	**11**
31	2	2	2	**6**	2	2	2	**6**	**12**
32	2	2	2	**6**	2	2	1	**5**	**11**
33									**No results submitted**
34	2	2	2	**6**	2	2	2	**6**	**12**
35	2	0	2	**4**	2	0	2	**4**	**8**
36	2	2	2	**6**	2	2	2	**6**	**12**
37	2	2	2	**6**	2	2	2	**6**	**12**
38	2	2	2	**6**	2	2	1	**5**	**11**
39	2	2	2	**6**	2	2	2	**6**	**12**
40	2	2	2	**6**	2	2	2	**6**	**12**
41	2	0	2	**4**	2	0	2	**4**	**8**
42	2	2	2	**6**	2	2	2	**6**	**12**

Sample ID / Lab ID	Technical				Advice				Total score (Max 12)
	D	E	F	Total	D	E	F	Total	
Average score	1.96	1.82	1.94		1.80	1.76	1.71		
43	2	2	2	**6**	2	2	2	**6**	**12**
44	2	2	2	**6**	2	2	1	**5**	**11**
45	2	2	2	**6**	2	2	2	**6**	**12**
46	2	2	2	**6**	1	2	2	**5**	**11**
47									**No results submitted**
48	2	2	2	**6**	2	2	2	**6**	**12**
49									**No results submitted**
50	2	0	0	**2**	2	0	0	**2**	**4**
51	2	2	2	**6**	2	2	2	**6**	**12**
52									**No results submitted**
53	2	2	2	**6**	2	2	2	**6**	**12**
54	2	2	2	**6**	2	2	1	**5**	**11**
55	0	2	1	**3**	0	1	1	**2**	**5**
56	2	2	2	**6**	2	2	2	**6**	**12**
57	2	2	2	**6**	2	2	2	**6**	**12**

APPENDIX 2. Change log (changes since the last version)

Version Number	Published	Amendments
1	20 November 2025	• 2025 Second round interim report published

END OF REPORT